## REMARKS

Claims 84, 85, 89-93 and 95-114 are pending following the amendment submitted herein. Claims 84, 91, 92, 95, 100, 101 and 105 have been amended. The marked up version of the claim amendments is attached hereto and is captioned "Version with Markings to Show Changes Made."

### I. Interview Summary.

Applicants wish to express their appreciation for the time and courtesy extended by Examiner Lucas and Supervisory Primary Examiner Housel during the telephonic interview of 16 April 2003 in connection with this application. During the interview, the outstanding rejections were discussed.

### II. Amendments to the Claims.

Claims 84, 91, 92, 95, 100, 101 and 105 have been amended to recite a "naturally occurring" cancer cell antigen. Applicants note for the record that these are not narrowing amendments. Support for this claim language is found at page 7 (line 6) and at page 17 (line 31) of the specification as originally filed.

Accordingly, Applicants submit that the claim amendments are supported by the application as filed and respectfully request entry thereof.

As discussed during the telephonic interview, the term "naturally occurring" more clearly recites the features of the invention and more clearly distinguishes the claimed invention from the artificial antigens of Falo et al. Falo et al. administer an artificial antigen to invoke a protective immune response to a different cancer cell antigen by cross-priming. In contrast, the compositions of the present invention provide an antigen that is the same as, or antigenically similar to, an antigen that is expressed by the cancer cell.

It was further discussed in the telephonic interview that any cancer specific protein (*e.g.*, Her2) contains a plurality of antigens (*i.e.*, epitopes), and th compositions of th present invention may encod one or more of these antigens.

Further, the issu of whether a "naturally occurring" cancer antigen according to the present invention may be altered was discussed during the telephonic interview. Applicants state for the record that a "naturally occurring" cancer antigen may be altered; for example, it may be isolated from the full-length protein, it may be combined with other peptides in a fusion protein, and/or it may include some mutations as long as it retains sufficient antigenic properties so that it can invoke a protective immune response against a cancer cell expressing the unaltered antigen.

III. **Investigations with other Cancer Antigens.**

During the course of the telephonic interview, data concerning cancer antigens other than Her2 were discussed. With respect to published studies, Applicants enclose herewith a paper by Velders et al., (2001) *Cancer Research* **61**:7861 and an abstract by Gardner et al., presented at the 2002 Keystone Symposia.

The investigations described in the Velders et al. paper were carried out by the laboratory of Dr. Martin Kast at Loyola University. Dr. Kast is a senior researcher in the field and is Director of the Cardinal Bernardin Cancer Center at Loyola.

The studies by Velders et al. demonstrate both prevention of tumor formation and tumor regression in a murine $E7^+$ model of cervical tumors following treatment with a VEE replicon expressing the human papilloma virus (HPV) E7 protein (*see, e.g.*, Abstract). Cervical cancer has been correlated with infection with HPV. In the E7+ model, C3 tumor cells that express the HPV E7 protein are transferred into C57/B16 mice. The mice develop tumors at the site of tumor cell inoculation (in this study, in the flanks). The E7+ model is considered state-of-the-art in the cervical cancer field.

The Gardner et al. abstract from the Keystone meetings demonstrates a strong cellular and humoral immune response against prostate-specific membrane antigen (PSMA) following administration of VEE replicon particles xpressing PSMA to an animal mod l of prostate cancer.

PMSA is specifically up-regulated in a splice-variant form on nearly all prostate cancer cells but not on normal tissues. Immune response was assessed by as determined by a panel of cellular and humoral immunoassays. The cellular responses were TH1 biased, which is believed to be advantageous for cancer vaccines approaches. Further, the cellular responses were relatively stable and were observed up to several months following vaccination. Gardner et al. concluded by stating that these data "strongly support the advancement of this novel vector system into human clinical testing."

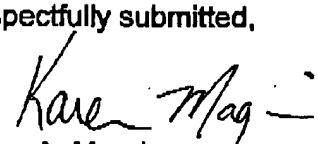
These studies were performed in a human HLA-A2 transgenic mouse model, which is considered to be the current state-of-the art animal model for prostate cancer as it is more relevant for assessing human Class I-restricted cellular responses. HLA-A2 is the most common human MHC class I molecule. This animal model was generated so that cellular immune response could be observed in a context that better reflected the immune response of human subjects to the antigen. Thus, mice which are transgenic for the human HLA-A2 molecule can be used to measure a cellular immune response in the context of a human MHC molecule.

In summary, the Velders et al. and Gardner et al. publications further support the enablement of the present claims.

## IV. Conclusions.

The points and concerns raised by the Examiner in the outstanding Office Action having been addressed in full, it is respectfully submitted that this application is in condition for allowance, which action is respectfully requested.

Respectfully submitted,



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Enclosures: Veld rs et al.
Gardner et al.

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Sloan Hobbs

**V rsion with Markings to Show Changes Made**

Please amend the claims as follows:

84. (Amended five times) A composition comprising infectious alphavirus particles in an immunogenically effective amount to prevent or treat cancer, wherein said alphavirus particles comprise one or more heterologous nucleotide sequences encoding a naturally occurring [native] cancer cell antigen; and wherein said alphavirus particles infect antigen-presenting cells, and further wherein said alphavirus particles comprise one or more attenuating mutations.

91. (Amended) The composition of Claim 84, wherein said naturally occurring [native] cancer antigen is selected from the group consisting of a helper T cell epitope, a cytotoxic T cell epitope, a T-dependent B cell epitope, and a T-independent B cell epitope.

92. (Amended) The composition of Claim 84, wherein said naturally occurring cancer antigen is a cell-surface protein or peptide.

95. (Amended four times) A composition comprising infectious Venezuelan Equine Encephalitis (VEE) particles in an immunogenically effective amount to prevent or treat cancer, wherein said VEE particles comprise one or more heterologous nucleotide sequences encoding a naturally occurring [native] cancer cell antigen; and wherein said VEE particles infect antigen-presenting cells, and further wherein said VEE particles comprise one or more attenuating mutations.

100. (Amended) The composition of Claim 95, wherein said naturally occurring [native] cancer antig n is s lected from the group

consisting of a helper T cell epitope, a cytotoxic T cell epitope, a T-dependent B cell epitope, and a T-independent B cell epitope.

101. (Amended) The composition of Claim 95, wherein said naturally occurring cancer antigen is a cell-surface protein or peptide.

105. (Amended) A composition comprising infectious alphavirus replicon particles in an immunogenically effective amount to prevent or treat cancer, wherein said alphavirus particles comprise one or more heterologous nucleotide sequences encoding a naturally occurring [native] cancer cell antigen, and wherein said alphavirus particles infect antigen-presenting cells.

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